REMARKS

The Invention

The invention is based on the identification of T-cell epitopes in Japanese pollen allergen molecules. Thus, the invention features peptides containing the T-cell epitopes and compositions containing the peptides that are useful in immunotherapy of patients with spring tree pollinosis. The peptides are also useful for diagnosis of spring tree pollinosis.

Status of the Claims

After entry of the amendments made herein, claims 1, 2, 5, 7, 11, 13, 14, 17, and 20-39 will be pending, and claims 1, 5, 29-35, 38, and 39 will be under consideration in this application, claims 2, 7, 11, 13-14, 17, 20-28, 36 and 37 having been withdrawn as allegedly being drawn to separate inventions.

No new matter is added by any of the amendments made herein to the claims.

Claim Objections

In response to the comment in paragraph 7 on page 3 of the Office Action, Applicants have added SEQ ID NOs to claims 29-31. These amendments are supported by the specification, e.g., at pages 9-10.

In paragraph 14 on page 9 of the Office Action, the Examiner indicates that, if written in independent form, claims 29-31 and 33-35 would be allowable. However, in paragraph 8 on page 3 of the Office Action, the Examiner has rejected claims 33-35 on the grounds that they allegedly contain new matter. Thus Applicants assume that, prior to the present Amendment and Response, the Examiner considered that only claims 29-31, if in independent form, would be allowable. Clarification is requested.

35 U.S.C. §112, first paragraph, rejections

(a) Claims 5 and 33-35 are rejected on the grounds that the term "consisting essentially of" allegedly has no support in the specification as filed. Applicants respectfully traverse this rejection.

The Examiner's attention is drawn to the Section 2111.03 of the MPEP that states in relevant part:

> The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. . . .For search and examination purposes, absent a clear indication in the specification of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." (Underlining in original)

Applicants submit that the specification, as a whole, makes it abundantly clear what "the basic and novel characteristics" of the present invention are. For example, the first sentence of the paragraph beginning on page 5, line 22, states that:

> [a]n objective of the present invention is to provide T-cell epitope peptides useful for peptide-based immunotherapy for Japanese cypress pollinosis. Another objective of the present invention is to provide T-cell epitope peptides useful for peptide-based immunotherapy for patients with pollinosis caused by tree pollens in springtime including patients with cedar pollinosis who show a cross-reactivity with Japanese cypress pollens.

The specification then lists the actual T-cell epitope peptides (with appropriate SEQ ID NOS) of the invention (pages 9-10). In light of this disclosure, one of skill in the art would understand that the "basic and novel characteristics" of the instant invention are T-cell epitope peptides useful for peptide-based immunotherapy for Japanese cypress pollinosis or pollinosis caused by other pollens (e.g., cedar pollen) that is cross-reactive with Japanese cypress pollinosis." Such a person would hence conclude that the term "consisting essentially of" excludes from the claimed compositions only T-cell epitope peptides useful for peptide-based immunotherapy of Japanese cypress pollinosis, or pollinoses cross-reactive with Japanese cypress pollinosis, other than the T-cell epitiope peptides listed in the claims to which the rejected claims refer, i.e., claims 1, 29, 30, and 31

Furthermore, Applicants submit that, in view of the text on page 13, line, 27, to page 14, line 4, of the specification ("The T-cell epitope peptide of the present invention may be used in combination with other peptides such as a T-cell epitope peptide of Cry j 1 (JP-WA-Hei 8-502163) and/or a T-cell epitope peptide of Cry j 2 (JP-WA-Hei 8-47392)"), one of skill in the art

would understand the term "consisting essentially of" used in claims 5 and 33-35 to mean that the compositions specified by the claims do not contain any therapeutic peptide other than the ones specified in those claims.

(b) Claims 1, 5, 32, 38, and 39 stand rejected on the grounds that the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims. Applicants respectfully traverse this rejection.

Claims 1 and 39 have been amended to specify that: (a) peptides consisting of the amino acid sequences listed in the two claims have T-cell stimulating activity; and (b) peptides consisting of parts of the amino acid sequences listed in the two claims have T-cell stimulating activities equivalent to the stimulating activities of the peptides consisting of the listed amino acid sequences. These amendments are supported by the specification, e.g., at page 7, line 27, to page 8, line 26, and page 11, lines 3-12.

From the comments on page 3, line 28, to page 7, line 12, of the Office Action, Applicants understand the Examiner's position to be that it would involve undue experimentation for one of skill in the art to identify parts of the amino acid sequences listed in the claim 1 that would bind to major histocompatibility complex (MHC) class II molecules and activate T-cells. Applicants disagree with this position.

What is required by the instant claims is that peptide epitopes (we'll call them "parent peptides") have the ability to stimulate T-cells and that the parts of the parent peptides ("peptide parts") have T-cell stimulating activity equivalent to that of the corresponding parent peptides. The claims specify 25 different parent peptides with an average length of about 15 amino acids. In order to activate T-cells, it is necessary for a peptide to first bind to a MHC molecule (in the present case, a MHC class II molecule). As acknowledged by the Examiner (page 5, lines 18-20, of the Office Action), peptides that bind to MHC class II molecules are generally at least about 10 amino acids long. In order to identify parts of one of the parent peptides of the invention that have T-cell stimulating activity equivalent to the corresponding parent peptide, one of skill in the art would know to sequentially delete, one at a time, amino acids from either end of the parent peptide (see, for example, page 11, lines 2-8, of the specification) and, in this

way, derive from the parent peptide a panel of peptide parts of appropriate length. These peptide parts would then be compared by methods known in the art (e.g., those described in Example 5 and page 8 of the specification) with the parent peptide for their ability to activate T-cells in the presence of MHC class II molecules of interest. Given that the difference between the average length of the parent peptides of the invention and the minimum length of a peptide that is required for binding to MHC class II molecules is only about 5-8 amino acids, the experimentation required to identify peptide parts that have T-cell stimulating activity equivalent to the corresponding parent peptide would be entirely routine and thus not undue. The Examiner is reminded that:

> a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable guidance with respect to the direction in which experimentation should proceed. *In re Wands*, 858 F.2d 731, 736-7 (Fed. Cir. 1988)

With respect to the comments on page 5, lines 6-17, of the Office Action, Applicants submit that it is not necessary to test the peptide parts for their ability to bind to MHC class II molecules. All that is necessary (and is required by the claims) is that the peptide parts have T-cell stimulating activity equivalent to that of the parent peptide. If a peptide activates T-cells, it is implicit that it has bound to MHC molecules, in the present case MHC class II molecules. Moreover, while the claims do not require that the peptide parts activate the production of interferon-γ (IFN-γ) by T-cells, having identified peptides that activate T-cells (by, example, a cell proliferation assay), it would be a simple matter to identify those that elicit the production of IFN-γ by T-cells. If desired, no initial cell proliferation assay need be performed; the assay used to screen a panel of peptide parts for those that have T-cell stimulating activity equivalent to the appropriate parent peptide could be an assay for IFN-γ production. Moreover, the parent peptide and peptide parts could easily be tested by well-established methodologies for their relative ability to stimulate the production of any of a number of cytokines involved in the regulation of allergic responses (see comments on page 5, line 25, to page 7, line 6, of the Office Action).

Applicants submit that the addition of the above-described functional limitations to claims 1 and 39 renders moot the Examiner's objection (in terms of vagueness) to the term "part" (page 5, lines 14-17, of the Office Action). In that the claims as amended above require that the

parent peptides stimulate T-cells and that the peptide parts have T-cell stimulating activity equivalent to that of the parent peptides, the length of the peptide parts would necessarily be between the length of the parent peptide and the length necessary for a peptide to bind to MHC class II molecules (see above).

(c) Claims 1, 5, 32, 38, and 39 are rejected on the grounds that they allegedly contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this rejection.

From the comments on page 7, line 17, to page 8, line 22, of the Office Action, Applicants understand the Examiner's position to be that the specification does not provide adequate written description of the peptide parts as specified by the instant claims. Applicants disagree with this position and submit that adequate written description is provided by the following sections of the application as originally filed.

First, claims 1 and 2 as originally filed, in addition to specifying parent peptides, specified parts of the parent peptides. In addition, the specification explicitly recites the minimum size of the peptides of the invention (e.g., at page 13, lines 21-22). Moreover, for the reasons given above, the requirement that the peptide parts have T-cell stimulatory activity equivalent to that of the parent peptide puts a limit on how small the peptides can be; they cannot be, for example, one or two amino acids in length (Office Action, page 8, lines 11-15). Applicants respectfully submit that, given this disclosure on peptide size and function and the amino sequences of the parent peptides (Sequence Listing and Figures 2-4 and 6-8), the application would convince one skilled in the art that, at the time the application was filed, the inventors had possession of the claimed invention as it relates to peptide parts.

In light of the above considerations, Applicants respectfully request that the rejections under 35 U.S.C. §112, first paragraph, be withdrawn.

35 U.S.C. §112, second paragraph, rejection

Claim 32 is rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention.

In response to the Examiner's comments on page 8, lines 29-31, of the Office Action, claim 32 has been amended to correctly refer to claim 5. This amendment is supported by the specification, e.g., at page 5, line 22, to page 6, line 2; page 15, lines 11-24; and page 21, lines 3-11.

In light of this consideration, Applicants request withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

Attached is a marked-up version of the changes being made by the current amendment.

CONCLUSION

In summary, for the reasons set forth above, Applicants maintain that the pending claims patentably define the invention. Applicants request that the Examiner reconsider the rejections as set forth in the Office Action, and permit the claims under consideration to pass to allowance.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicants' undersigned representative can be reached at the telephone number listed below.

Enclosed is a Petition for Extension of Time with the required fee. Please charge any other fees or make any credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 06501-024001.

Respectfully submitted,

Date: 2/13/03

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Version with markings to show changes made

In the claims:

Claims 1, 29-32, and 39 have been amended as follows:

1. (Three times amended) A peptide consisting of at least one T-cell epitope of Japanese cypress pollen allergen Cha o 1, [and optionally a linker sensitive to enzyme cleavage between two epitopes,] wherein each of said epitopes consists of:

(a) an amino acid sequence selected from the group consisting of Peptide #1-2 (SEQ ID NO:4), Peptide #1-4 (SEQ ID NO:6), Peptide #1-5 (SEQ ID NO:7), Peptide #1-6 (SEQ ID NO:8), Peptide #1-7 (SEQ ID NO:9), Peptide #1-8 (SEQ ID NO:10), Peptide #1-10 (SEQ ID NO:12), Peptide #1-11 (SEQ ID NO:13), Peptide #1-12 (SEQ ID NO:14), Peptide #1-14 (SEQ ID NO:16), Peptide #1-15 (SEQ ID NO:17), Peptide #1-16 (SEQ ID NO:18), Peptide #1-19 (SEQ ID NO:21), Peptide #1-20 (SEQ ID NO:22), Peptide #1-21 (SEQ ID NO:23), Peptide #1-22 (SEQ ID NO: 24), Peptide #1-23 (SEQ ID NO:25), Peptide #1-24 (SEQ ID NO:26), Peptide #1-25 (SEQ ID NO:27), Peptide #1-27 (SEQ ID NO:29), Peptide #1-30 (SEQ ID NO:32), Peptide #1-31 (SEQ ID NO:33), Peptide #1-32 (SEQ ID NO:34), Peptide #1-33 (SEQ ID NO:35), and Peptide #1-34 (SEQ ID NO:36) shown in Fig. 4[,] and has T-cell stimulating activity; or

(b) a part of said amino acid sequence and has T-cell stimulating activity equivalent to that of a peptide consisting of said amino acid sequence.

29. (Amended) The peptide of claim 1, wherein each of said epitopes consists of an amino acid sequence selected from the group consisting of: Peptide #1-2 (SEQ ID NO:4), Peptide #1-4 (SEQ ID NO:6) , Peptide #1-5 (SEQ ID NO:7), Peptide #1-6 (SEQ ID NO:8), Peptide #1-7 (SEQ ID NO:9), Peptide #1-8 (SEQ ID NO:10), Peptide #1-10 (SEQ ID NO:12), Peptide #1-11 (SEQ ID NO:13),Peptide #1-12 (SEQ ID NO:14), Peptide #1-14 (SEQ ID NO:16), Peptide #1-15 (SEQ ID NO:17), Peptide #1-16 (SEQ ID NO:18), Peptide #1-19 (SEQ ID NO:21), Peptide #1-20 (SEQ ID NO:22), Peptide #1-21 (SEQ ID NO:23), Peptide #1-22 (SEQ

ID NO:24), Peptide #1-23 (SEQ ID NO:25), Peptide #1-24 (SEQ ID NO:26), Peptide #1-25 (SEQ ID NO:27), Peptide #1-27 (SEQ ID NO:29), Peptide #1-30 (SEQ ID NO:32), Peptide #1-31 (SEQ ID NO:33), Peptide #1-32 (SEQ ID NO:34), Peptide #1-33 (SEQ ID NO:35) and Peptide #1-34 (SEQ ID NO:36) shown in Fig. 4.

30. (Amended) The peptide of claim 1, wherein each of said epitopes consists of an amino acid sequence selected from the group consisting of Peptide #1-2 (SEQ ID NO:4), Peptide #1-7 (SEQ ID NO:9), Peptide #1-8 (SEQ ID NO:10), Peptide #1-20 (SEQ ID NO:22), Peptide #1-22 (SEQ ID NO:24), Peptide #1-24 (SEQ ID NO:26), Peptide #1-32 (SEQ ID NO:34), Peptide #1-33 (SEQ ID NO:35), and Peptide #1-34 (SEQ ID NO:36) shown in Fig. 4.

31. (Amended) The peptide of claim 1, wherein each of said epitopes consists of an amino acid sequence selected from the group consisting of Peptide #1-7 (SEQ ID NO:9), Peptide #1-22 (SEQ ID NO:24), Peptide #1-32 (SEQ ID NO:34), and Peptide #1-33 (SEQ ID NO:35) shown in Fig. 4.

32. (Amended) The composition of claim 5, wherein treatment of a patient with said [pollinosis] composition [is] can reduce the symptoms of Japanese cypress pollinosis [and/] or cedar pollinosis.

39. (Amended) A peptide consisting of at least two T-cell epitopes of Japanese cypress pollen allergen Cha o 1 and a linker sensitive to enzyme cleavage between two T-cell epitopes, wherein at least one of said epitopes consists of:

(a) an amino acid sequence selected from the group consisting of Peptide #1-2 (SEQ ID NO:4), Peptide #1-4 (SEQ ID NO:6), Peptide #1-5 (SEQ ID NO:7), Peptide #1-6 (SEQ ID NO:8), Peptide #1-7 (SEQ ID NO:9), Peptide #1-8 (SEQ ID NO:10), Peptide #1-10 (SEQ ID NO:12), Peptide #1-11 (SEQ ID NO:13), Peptide #1-12 (SEQ ID NO:14), Peptide #1-14 (SEQ ID NO:16), Peptide #1-15 (SEQ ID NO:17), Peptide #1-16 (SEQ ID NO:18), Peptide #1-19 (SEQ ID NO:21), Peptide #1-20 (SEQ ID NO:22), Peptide #1-21 (SEQ ID NO:23), Peptide #1-22 (SEQ ID NO: 24), Peptide #1-23 (SEQ ID NO:25), Peptide #1-24 (SEQ ID NO:26), Peptide

#1-25 (SEQ ID NO:27), Peptide #1-26 (SEQ ID NO:28), Peptide #1-27 (SEQ ID NO:29), Peptide #1-30 (SEQ ID NO:32), Peptide #1-31 (SEQ ID NO:33), Peptide #1-32 (SEQ ID NO:34), Peptide #1-33 (SEQ ID NO:35), and Peptide #1-34 (SEQ ID NO:36) shown in Fig. 4[,] and has T-cell stimulating activity; or

(b) a part of said amino acid sequence and has T-cell stimulating activity equivalent to that of a peptide consisting of said amino acid sequence.